Presence of a putative tumor-initiating progenitor cell population predicts poor prognosis in smokers with non-small cell lung cancer.

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Public Summary:
Smoking is the most important known risk factor for the development of lung cancer. Tobacco exposure results in chronic inflammation, tissue injury and repair. A recent hypothesis argues for a stem/progenitor cell involved in airway epithelial repair that may be a tumor-initiating cell in lung cancer, and which may be associated with recurrence and spread of the disease. We identified a subpopulation of airway epithelial stem/progenitor cells that were important for repair of the airways. Under normal conditions these stem/progenitpr cells did not persist once the repair of the airway was complete. However, when abnormal repair occurred with the development of precancerous lesions, these stem/progenitor cells persisted. Furthermore, the presence of these stem/progenitor cells in non-small cell lung cancer samples predicted a worse prognosis for patients, even if they had small tumors that were completely surgically removed. The predictive value was strongest in smokers where it also correlated with spread of the disease. This suggests that this stem/progenitor cell population in the airway may be the tumor-initiating cell in smokers with non-small cell lung cancer.

Scientific Abstract:
Smoking is the most important known risk factor for the development of lung cancer. Tobacco exposure results in chronic inflammation, tissue injury, and repair. A recent hypothesis argues for a stem/progenitor cell involved in airway epithelial repair that may be a tumor-initiating cell in lung cancer and which may be associated with recurrence and metastasis. We used immunostaining, quantitative real-time PCR, Western blots, and lung cancer tissue microarrays to identify subpopulations of airway epithelial stem/progenitor cells under steady-state conditions, normal repair, aberrant repair with premalignant lesions and lung cancer, and their correlation with injury and prognosis. We identified a population of keratin 14 (K14)-expressing progenitor epithelial cells that was involved in repair after injury. Dysregulated repair resulted in the persistence of K14+ cells in the airway epithelium in potentially premalignant lesions. The presence of K14+ progenitor airway epithelial cells in NSCLC predicted a poor prognosis, and this predictive value was strongest in smokers, in which it also correlated with metastasis. This suggests that reparative K14+ progenitor cells may be tumor-initiating cells in this subgroup of smokers with NSCLC.